response (CR), 2 partial responses (PR), and 8 patients with stable disease (SD). The patient with the CR has been maintained on BIBF 1120 monotherapy for a period of over 52 weeks.

Conclusions: The combination of BIBF 1120 and pemetrexed in previously treated NSCLC patients was shown to be safe and well tolerated in this study. The MTD of BIBF 1120 was 200 mg bid when given with pemetrexed at 500 mg/m^2. Signs of clinical efficacy were observed in the small number of patients treated in this trial.

P3-092 NSCLC: Molecular Targeted Therapy Posters, Wed, Sept 5 – Thurs, Sept 6

Recent Southwest Oncology Group (SWOG) trials in Performance Status (PS) 2 patients with advanced non-small cell lung cancer (NSCLC)

Hesketh, Paul J.[1] Chansky, Kari[2] Lau, Derick H.[3] Wozniak, Antoinette J.[4] Lara, Primo[3] Crowley, John[2] Gandara, David R.[3]

[1] Division of Hematology Oncology Caritas St. Elizabeth's Medical Center of Boston, Boston, MA, USA [2] Cancer Research and Biostatistics, Seattle, WA, USA [3] University of California Davis Cancer Center, Sacramento, CA, USA [4] Karmanos Cancer Institute, Detroit, MI, USA

Background: Advanced stage NSCLC patients (pts) with a PS of 2 have inferior outcomes compared to good PS pts. No consensus exists on the most appropriate management approach, with options ranging from supportive care alone to platinum-based combination chemotherapy. SWOG has recently completed two trials (S0027) and (S0341) evaluating the value of sequential single agent chemotherapy and the EGFR tyrosine kinase inhibitor erlotinib (E) respectively in unselected pt populations with PS 2. This report details a comparative analysis of these two treatment approaches.

Methods: Eligibility: stage III B (pleural effusion)/IV NSCLC; PS 2; measurable disease (S0341), measurable + evaluable disease (S0027); no prior chemotherapy/biologic treatment. Pts > age 70 with PS 0-1 also eligible for S0027 but this strata not included in this analysis. Treatment: (S0027) vinorelbine 25 mg/m^2 d 1,8 q 21 d for 3 cycles then docetaxel 35 mg/m^2 d1,8,15 q 28 d for 3 cycles; (S0341) E 150 mg orally daily.

Results: (S0027, S0341): Eligible patients: 42, 73; median age 73, 74; M/F (%) 55/45, 47/53; stage IIIB/IV (%) 15/85, 12/88, respectively. Response rate (RR), disease control rate{response + stable disease} (DCR), progression free survival (PFS), median survival (MST) and toxicity - see table.

Conclusions: Outcome with sequential single agent chemotherapy or single agent erlotinib remains poor in advanced NSCLC pts with PS 2. Overall tolerance of treatment appeared to be more favorable in pts receiving erlotinib. Better patient selection employing an EGFR biomarker strategy may improve results with E and result in a superior outcome to chemotherapy in this selected patient population. This concept is now being explored within SWOG.

	S0027(N=42)	S0341(N=73)
Response Rates: Complete/Partial	0%/11% (N=37)	1%/7% (N=72)
Disease Control Rate: Response+Stable Disease	38% (N=37)	43% (N=72)
PFS/MST (95% C I)	2.6(1.9-4.2)/ 5.5(3.1-6.5)	2.1(1.5-3.1)/ 5(3.5-7.3)
Grade 3/4 AE's(%)	48/26	33/7
Grade 5 AE(%)	4.8	1.4

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Correlative analyses of plasma cytokine / angiogenic factor (C/AF) profile, gender and outcome in a randomized, three-arm, phase II trial of 1st-line vandetanib (VAN) and / or carboplatin plus paclitaxel (CP) for advanced non small cell lung cancer (NSCLC).

Heymach, J V.[1] Hanrahan, E O.[1] Lin, H Y.[1] Du, D Z.[1] Yan, S[1] Kim, E S.[1] Lee, J J.[1] Ryan, A J.[2] Tran, H T.[1] Johnson, B E.[3]

[1] University of Texas M.D. Anderson Cancer Center, Houston, TX, USA [2] AstraZeneca, Macclesfield, UK [3] Dana-Farber Cancer Institute, Boston, MA, USA

Background: VAN (ZD6474) is an oral inhibitor of VEGFR, EGFR and RET. In a phase II trial, 181 patients with advanced NSCLC were randomized to 1st-line treatment with VAN, CP or VAN + CP. Progression free survival (PFS) was prolonged for VAN + CP vs CP (Heymach et al, Proc ASCO 2007). Exploratory subgroup analyses suggest gender differences in PFS benefit for VAN + CP vs CP (HR 0.47 in females vs 1.05 in males). We performed exploratory analyses of plasma levels of 35 C/AFs to investigate gender differences and potential prognostic or predictive markers.

Methods: Plasma was collected at baseline (n = 123; VAN 55, CP 32, VAN + CP 36), day (D) 8 (n = 104), D22 (n = 95), and D43 (n = 83). We used multiplex bead assays to measure 33 plasma C/AFs, including VEGF, basic FGF, EGF, HGF, E-selectin, ICAM-1, MMP-9, multiple chemokines and interleukins (IL). Osteopontin and sVEGFR-2 were measured by ELISA. Cox models were applied on PFS to identify prognostic / predictive markers after rank transformation and adjusted for covariates.

Results: Significant gender differences in baseline C/AF levels were seen for IL-15, IL-1RA, IL-2R, MIG, and MIP-1α (all higher in females, all p <.022). During treatment, significant changes in median VEGF levels (102 pg/mL at baseline, 127 pg/mL at day 43, p = .041) and sVEGFR-2 levels (9593 pg/mL at baseline, 7696 pg/mL at day 43, p = .027) occurred in the VAN arm. IL-12, IL-1RA, MMP-9 and MCP-1 levels were modulated in the CP and VCP arms. High baseline E-selectin (p = .01), IL-6 (p = .018), and sIL-2R (p = .008) were negative prognostic indicators for PFS. Tests for treatment by factor interactions (assessing if treatment effect was different in patients with low and high levels of a factor), including all 3 treatment arms, were significant for baseline HGF (p = .04) and sIL-2R (p = .008). Low levels of HGF and sIL-2R were predictive of prolonged PFS in the VAN arm, but not in the CP or VAN+CP arms. When only the VAN+CP and CP arms were considered, the tests for treatment by factor interaction were of borderline significance for baseline ICAM-1, sVEGFR-2, MMP-9 and EGF. Low ICAM-1, sVEGFR-2, and MMP-9, and high EGF were associated with greater PFS in the VCP arm, but not in the CP arm.

Conclusions: There are gender differences in PFS benefit from VAN and in plasma C/AF profile. Several C/AFs were of prognostic value, whereas low HGF and IL-2R were predictive of benefit in the VAN but not CP and VAN + CP arms. This study suggests that broad-based plasma profiling of cytokines and angiogenic factors may be feasible approach for identifying prognostic and predictive markers of benefit for different therapies. Further investigation of these biomarkers is warranted.